

Bias-exchange metadynamics simulations: an efficient strategy for the analysis of conduction and selectivity in ion channels

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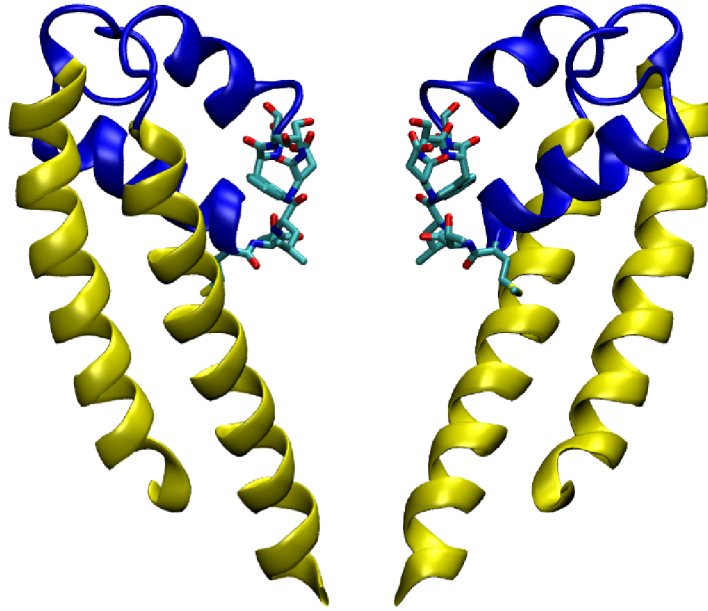


Figure S1. Model System. Two opposing subunits of the NaVAb channel (3RVY.pdb) out of four are shown in cartoon representation. Only the pore region of the channel is shown, from residue 129 to residue 221; these correspond to transmembrane helices S5 and S6. The model system included the portion of the protein from residue 154 to residue 193 (in blue). Residues of the selectivity filter are shown in licorice representation.

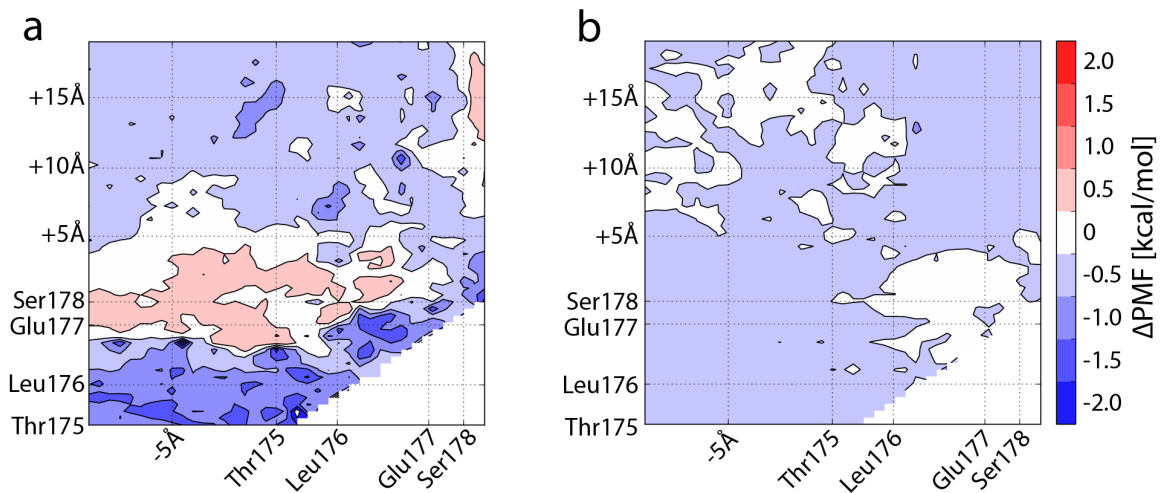


Figure S2. Difference between PMF maps estimated with umbrella sampling simulations of different length. ΔPMF was defined as the PMF calculated with umbrella sampling simulations of (a) 0.5 ns minus the PMF calculate with umbrella sampling simulations of 0.25 ns, and (b) 2.0 ns minus the PMF calculated with umbrella sampling simulations of 1.75 ns.

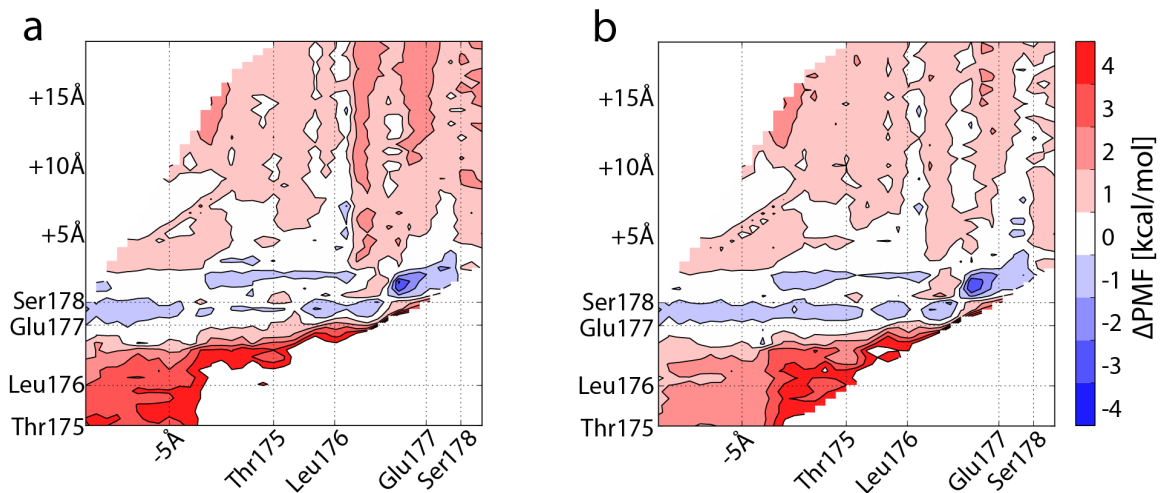


Figure S3. Difference between PMF maps estimated with BE-meta simulations and with umbrella sampling simulations of different length. ΔPMF was defined as the PMF calculated with umbrella sampling simulations of 0.5 ns (a) and 2.0 ns (b) minus the PMF calculated by the BE-meta simulation BE_2NA.

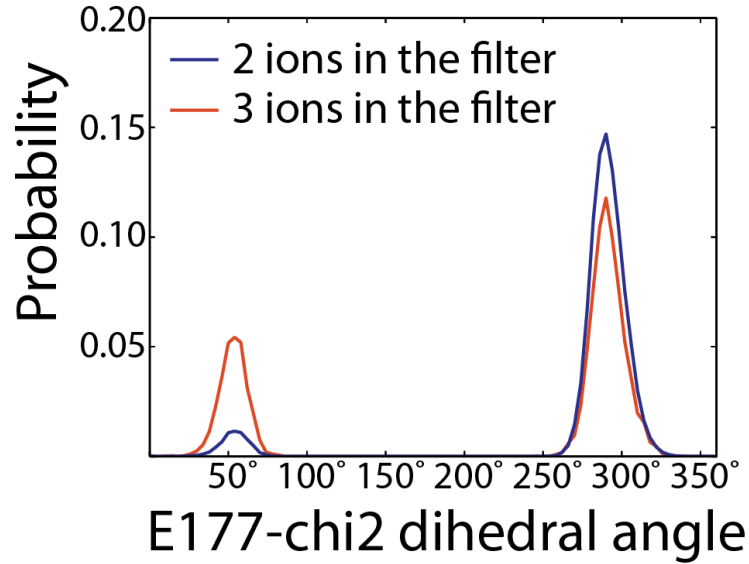


Figure S4. Configurations of residues E177. Probability distribution of the chi2 dihedral angle ($C_{\alpha}-C_{\beta}-C_{\gamma}-C_{\delta}$) of residues E177 in the presence of 2 Na^+ ions (blue line) or 3 Na^+ ions inside the selectivity filter ($0.0 \text{ \AA} \leq CV \leq 1.1 \text{ \AA}$). The carbonyl oxygen atoms of E177 are directed towards the extracellular side when chi2 is $\sim 300^\circ$, while they point to the pore lumen when chi2 is $\sim 50^\circ$. Data were collected from the BE-meta simulation BE_4NA.